L2: Entry 1 of 1 File: USPT Apr 13, 2004

US-PAT-NO: 6719974
DOCUMENT-IDENTIFIER: US 6719974 B1

TITLE: Heat shock protein-based vaccines and immunotherapies

DATE-ISSUED: April 13, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rothman; James E.	New York	NY		
Hartl; Franz Ulrich	Kottgeisering			DE
Hoe; Mee H.	Irvington	NY		
Houghton; Alan	New York	NY		
Takeuchi; Yoshizumi	Kobe			JP
Mayhew; Mark	New York	NY		

US-CL-CURRENT: 424/185.1; 424/193.1, 424/195.11, 424/196.11, 424/197.11, 424/277.1, 424/278.1, 514/2, 514/24, 530/412, 530/413, 530/828

CLAIMS:

What is claimed is:

1. A method of treating melanoma, comprising administering to a subject an effective amount of a complex of: (a) a hybrid antigen comprising an antigenic domain of a tumor antigen from melanoma and a binding domain that noncovalently binds to a eukaryotic hsp70 and comprises a heptameric region having the sequence motif HyXHyXHyXHy (SEQ ID NO:29) where Hy represents a hydrophobic amino acid and X is any amino acid, wherein the antigenic domain and the binding domain are separated by a short peptide linker; and (b) the eukaryotic hsp70; wherein the hsp70 is from the same species as the subject; wherein the antigenic domain is from a first source and the binding domain is from a second source different from the first source; wherein the binding domain, the short peptide linker, and the antigenic domain are covalently bound in vitro; and wherein the hybrid antigen and the hsp70 are combined in vitro under conditions wherein binding of the hybrid antigen to the hsp70 occurs to form a non-covalent hybrid antigen-hsp70 complex.

2. The method of claim 1, wherein the hydrophobic amino acid is independently selected from the group consisting of tryptophan, leucine and phenylalanine.

3. The method of claim 1, wherein the binding domain comprises the sequence His Trp Asp Phe Ala Trp Pro Trp (SEQ ID NO: 1).

4. The method of claim 1, wherein the binding domain comprises the sequence Phe Trp Gly Leu Trp Pro Trp Glu (SEQ ID NO:4).

5. A method of treating melanoma, comprising administering to a subject an effective amount of a complex of: (a) a hybrid antigen comprising an antigenic domain of a tumor antigen from melanoma and a binding domain that comprises a hydrophobic peptide of 7-15 amino acids that non-covalently binds to a eukaryotic hsp70, wherein the antigenic domain and the binding domain are separated by a short peptide linker; and (b) the eukaryotic hsp70; wherein the hsp70 is from the same species as the subject; wherein the antigenic domain is from a first source and the binding domain is from a second source different from the first source; wherein the binding domain, the short peptide linker, and the antigenic domain are covalently bound in vitro; and wherein the hybrid antigen and the hsp70 are combined in vitro under conditions wherein binding of the hybrid antigen to the hsp70 occurs to form a non-covalent hybrid antigen-hsp70 complex.

6. The method of claim 5, wherein the binding domain comprises a heptameric region having the sequence motif HyXHyXHyXHy (SEQ ID NO:29) where Hy represents a hydrophobic amino acid and X is any amino acid.

7. The method of claim 6, wherein the hydrophobic amino acid is independently selected from the group consisting of tryptophan, leucine and phenylalanine.

8. The method of claim 6, wherein the binding domain comprises a region having the sequence His Trp Asp Phe Ala Trp Pro Trp (SEQ ID NO:1).

9. The method of claim 6, wherein the binding domain comprises a region having the sequence Phe Trp Gly Leu Trp Pro Trp Glu (SEQ ID NO:4).

10. The method of claim 1 or 5, wherein the short peptide linker is Gly-Ser-Gly.

11. The method of claim 1 or 5, wherein the hsp70 is mammalian.

12. A method of treating melanoma, comprising administering to a subject an effective amount of a complex of: (a) a hybrid antigen comprising an antigenic domain of a tumor antigen from melanoma and a binding domain that noncovalently binds to a eukaryotic heat shock protein selected from the group consisting of hsp70, hsc70, and BiP, and comprises a heptameric region having the sequence motif HyXHyXHyXHy (SEQ ID NO:29) where Hy represents a hydrophobic amino acid and X is any amino acid, wherein the antigenic domain and the binding domain are separated by a short peptide linker; and (b) the eukaryotic heat shock protein; wherein the heat shock protein is from the same species as the subject; wherein the antigenic domain is from a first source and the binding domain is from a second source different from the first source; wherein the binding domain, the short peptide linker, and the antigenic domain are covalently bound in vitro; and wherein the hybrid antigen and the heat shock protein are combined in vitro under conditions wherein binding of the hybrid antigen to the heat shock protein occurs to form a non-covalent hybrid antigen-heat shock protein complex.

13. The method of claim 12, wherein the hydrophobic amino acid is independently selected from the group consisting of tryptophan, leucine and phenylalanine.

14. The method of claim 12, wherein the binding domain comprises the sequence His Trp Asp Phe Ala Trp Pro Trp (SEQ ID NO:1).

15. The method of claim 12, wherein the binding domain comprises the sequence Phe Trp Gly Leu Trp Pro Trp Glu (SEQ ID NO:4).

16. A method of treating melanoma, comprising administering to a subject an effective amount of a complex of: (a) a hybrid antigen comprising an antigenic domain of a tumor antigen from melanoma and a binding domain that comprises a hydrophobic peptide of 7-15 amino acids that non-covalently binds to a eukaryotic heat shock protein selected from the group consisting of hsp70, hsc70, and BiP, wherein the antigenic domain and the binding domain are separated by a short peptide linker; and (b) the eukaryotic heat shock protein; wherein the heat shock protein is from the same species as the subject; wherein the antigenic domain is from a first source and the binding domain is from a second source different from the first source; wherein the binding domain, the short peptide linker, and the antigenic domain are covalently bound in vitro; and wherein the hybrid antigen and the heat shock protein are combined in vitro under conditions wherein binding of the hybrid antigen to the heat shock protein occurs to form a non-covalent hybrid antigen-heat shock protein complex.

17. The method of claim 16, wherein the binding domain comprises a heptameric region having the sequence motif HyXHyXHyXHy (SEQ ID NO:29) where Hy represents a hydrophobic amino acid and X is any amino acid.

18. The method of claim 17, wherein the hydrophobic amino acid is independently selected from the group consisting of tryptophan, leucine and phenylalanine.

19. The method of claim 17, wherein the binding domain comprises a region having the sequence His Trp Asp Phe Ala Trp Pro Trp (SEQ ID NO:1).

20. The method of claim 17, wherein the binding domain comprises a region having the sequence Phe Trp Gly Leu Trp Pro Trp Glu (SEQ ID NO:4).

21. The method of claim 12 or 16, wherein the short peptide linker is Gly-Ser-Gly.

22. The method of claim 12 or 16, wherein the heat shock protein is mammalian.

23. A method of treating lymphoma, comprising administering to a subject an effective amount of a complex of: (a) a hybrid antigen comprising an antigenic domain of a tumor antigen from lymphoma and a binding domain that noncovalently binds to a eukaryotic hsp70 and comprises a heptameric region having the sequence motif HyXHyXHyXHy (SEQ ID NO:29) where Hy represents a hydrophobic amino acid and X is any amino acid, wherein the antigenic domain and the binding domain are separated by a short peptide linker; and (b) the eukaryotic hsp70; wherein the hsp70 is from the same species as the subject; wherein the antigenic domain is from a first source and the binding domain is from a second source different from the first source; wherein the binding domain, the short peptide linker, and the antigenic domain are covalently bound in vitro; and wherein the hybrid antigen and the hsp70 are combined in vitro under conditions wherein binding of the hybrid antigen to the hsp70 occurs to form a non-covalent hybrid antigen-hsp70 complex.

24. The method of claim 23, wherein the hydrophobic amino acid is independently selected from the group consisting of tryptophan, leucine and phenylalanine.

25. The method of claim 23, wherein the binding domain comprises the sequence His Trp Asp Phe Ala Trp Pro Trp (SEQ ID NO:1).

26. The method of claim 23, wherein the binding domain comprises the sequence Phe Trp Gly Leu Trp Pro Trp Glu (SEQ ID NO:4).

27. A method of treating lymphoma, comprising administering to a subject an effective amount of a complex of: (a) a hybrid antigen comprising an antigenic domain of a tumor antigen from lymphoma and a binding domain that comprises a hydrophobic peptide of 7-15 amino acids that non-covalently binds to a eukaryotic hsp70, wherein the antigenic domain and the binding domain are separated by a short peptide linker; and (b) the eukaryotic hsp70; wherein the hsp70 is from the same species as the subject; wherein the antigenic domain is from a first source and the binding domain is from a second source different from the first source; wherein the binding domain, the short peptide linker, and the antigenic domain are covalently bound in vitro; and wherein the hybrid antigen and the hsp70 are combined in vitro under conditions wherein binding of the hybrid antigen to the hsp70 occurs to form a non-covalent hybrid antigen-hsp70 complex.

28. The method of claim 27, wherein the binding domain comprises a heptameric region having the sequence motif HyXHyXHyXHy (SEQ ID NO:29) where Hy represents a hydrophobic amino acid and X is any amino acid.

29. The method of claim 28, wherein the hydrophobic amino acid is independently selected from the group consisting of tryptophan, leucine and phenylalanine.

30. The method of claim 28, wherein the binding domain comprises a region having the sequence His Trp Asp Phe Ala Trp Pro Trp (SEQ ID NO:1).

31. The method of claim 28, wherein the binding domain comprises a region having the sequence Phe Trp Gly Leu Trp Pro Trp Glu (SEQ ID NO:4).

32. The method of claim 23 or 27, wherein the short peptide linker is Gly-Ser-Gly.

33. The method of claim 23 or 27, wherein the hsp70 is mammalian.

34. A method of treating lymphoma, comprising administering to a subject an effective amount of a complex of: (a) a hybrid antigen comprising an antigenic domain of a tumor antigen from lymphoma and a binding domain that noncovalently binds to a eukaryotic heat shock protein selected from the group consisting of hsp70, hsc70, and BiP, and comprises a heptameric region having the sequence motif HyXHyXHyXHy (SEQ ID NO:29) where Hy represents a hydrophobic amino acid and X is any amino acid, wherein the antigenic domain and the binding domain are separated by a short peptide linker; and (b) the eukaryotic heat shock protein; wherein the heat shock protein is from the same species as the subject; wherein the antigenic domain is from a first source and the binding domain is from a second source different from the first source; wherein the binding domain, the short peptide linker, and the antigenic domain are covalently bound in vitro; and wherein the hybrid antigen and the heat shock protein are combined in vitro under conditions wherein binding of the hybrid antigen to the heat shock protein occurs to form a non-covalent hybrid antigen-heat shock protein complex.

35. The method of claim 36, wherein the hydrophobic amino acid is independently selected from the group consisting of tryptophan, leucine and phenylalanine.

36. The method of claim 34, wherein the binding domain comprises the sequence His Trp Asp Phe Ala Trp Pro Trp (SEQ ID NO:1).

37. The method of claim 36, wherein the binding domain comprises the sequence Phe Trp Gly Leu Trp Pro Trp Glu (SEQ ID NO:4).

38. A method of treating lymphoma, comprising administering to a subject an effective amount of a complex of: (a) a hybrid antigen comprising an antigenic domain of a tumor antigen from lymphoma and a binding domain that comprises a hydrophobic peptide of 7-15 amino acids that non-covalently binds to a eukaryotic heat shock protein selected from the group consisting of hsp70, hsc70, and BiP, wherein the antigenic domain and the binding domain are separated by a short peptide linker; and (b) the eukaryotic heat shock protein; wherein the heat shock protein is from the same species as the subject; wherein the antigenic domain is from a first source and the binding domain is from a second source different from the first source; wherein the binding domain, the short peptide linker, and the antigenic domain are covalently bound in vitro; and wherein the hybrid antigen and the heat shock protein are combined in vitro under conditions wherein binding of the hybrid antigen to the heat shock protein occurs to form a non-covalent hybrid antigen-heat shock protein complex.

39. The method of claim 38, wherein the binding domain comprises a heptameric region having the sequence motif HyXHyXHyXHy (SEQ ID NO:29) where Hy represents a hydrophobic amino acid and X is any amino acid.

40. The method of claim 39, wherein the hydrophobic amino acid is independently selected from the group consisting of tryptophan, leucine and phenylalanine.

41. The method of claim 39, wherein the binding domain comprises a region having the sequence His Trp Asp Phe Ala Trp Pro Trp (SEQ ID NO:1).

42. The method of claim 39, wherein the binding domain comprises a region having the sequence Phe Trp Gly Leu Trp Pro Trp Glu (SEQ ID NO:4).

43. The method of claim 36 or 38, wherein the short peptide linker is Gly-Ser-Gly.

44. The method of claim 36 or 38, wherein the heat shock protein is mammalian.

Previous Doc Next Doc Go to Doc#